IFW

ATTORNEY'S DOCKET NUMBER: 2003946-0176

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Tsuruoka, *et al.*	Examiner: Not yet assigned
Serial Number:	10/521,074	Art Unit: 2829
Filed:	January 12, 2005	
Title:	NITROGEN-CONTAINING AROMATIC DERIVATIVES	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

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January 31, 2006
Date

Heather A. Mariacher
Signature

Heather A. Mariacher
Typed or Printed Name of person signing certificate

TRANSMITTAL LETTER

Enclosed please find the following documents regarding the above-referenced matter:

1) Request for Corrected Filing Receipt (2 pages);

2) Copy of Filing Receipt with corrections noted in red ink (2 pages);

3) Copy of Combined Declaration and Power of Attorney (4 pages);

4) Copy of the Preliminary Amendment as filed on January 12, 2005 (30 pages); and

5) This Return Postcard.

Please charge any fees or credit any overpayments to our Deposit Account No. 03-1721.

Respectfully submitted,

Date: January 31, 2006

C. Hunter Baker, M.D., Ph.D.
Registration Number: 46,533

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ATTORNEY DOCKET NO.: 2003946-0176

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Tsuruoka, *et al.*	Examiner:	To be assigned
Serial No.:	10/521,074	Art Unit:	1626
Filing Date:	January 12, 2005	International Application No.:	PCT/JP03/10964
		International Fling Date:	August 28, 2003
Title:	NITROGEN-CONTAINING AROMATIC DERIVATIVES		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

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January 31, 2006 _____ Heather A. Mariacher
Date Signature

Heather A. Mariacher
Typed or Printed Name of person signing certificate

REQUEST FOR CORRECTED FILING RECEIPT

Applicants respectfully request correction of the following errors in the filing receipt (copy attached with changes marked in red) for the above-referenced case:

1. One of the Applicants is listed as "Masayuki Matasukura"; the correct spelling is "Masayuki MATSUKURA." A copy of the Combined Declaration and Power of Attorney is enclosed verifying the correct legal name of the applicant.
2. Two applications to which the immediate application claims priority have been omitted under **Domestic Priority data as claimed by applicant**. Please insert the following:

   Japanese Patent Application 2002-253123, filed August 30, 2002; and

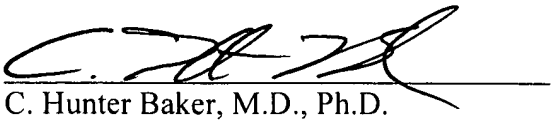
   U.S. Provisional Application 60/464,690, filed April 22, 2003.

   A copy of the Preliminary Amendment as filed on January 12, 2005 is enclosed in support of these priority claims.

Applicants respectfully request that a corrected filing receipt reflecting the corrections above be issued as soon as possible.

Please charge any fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully submitted,



C. Hunter Baker, M.D., Ph.D.
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Dated: January 31, 2006

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/521,074	01/12/2005	2829	4200	2003946-0176		46	1

Eisai

CONFIRMATION NO. 5420

Choate Hall & Stewart
Exchange Place
53 State Street
Boston, MA 02109-2891

FILING RECEIPT

OC000000016989638

Date Mailed: 09/15/2005

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please mail to the Commissioner for Patents P.O. Box 1450 Alexandria Va 22313-1450. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Akihiko Tsuruoka, Ibaraki, JAPAN;
Tomohiro Matsushima, Ibaraki, JAPAN;
Masayuki Matasukura, Ibaraki, JAPAN;
Kazuki Miyazaki, Ibaraki, JAPAN;
Keiko Takahashi, Ibaraki, JAPAN;
Junichi Kamata, Ibaraki, JAPAN;
Yoshio Fukuda, Ibaraki, JAPAN;

Power of Attorney:

Charles Baker--46533

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/JP03/10964 08/28/2003

Foreign Applications Japanese Patent Application 2002-253123, filed 08/30/02
U.S. Provisional application 60/464,690, filed 04/22/03.

Projected Publication Date: 12/22/2005

Non-Publication Request: No

Early Publication Request: No

Title

Nitrogen-containing aromatic derivatives

Preliminary Class

324

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

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Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

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No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

CHOATE, HALL & STEWA

Attorney's Docket No. 2003946-0176

Combined Declaration and Power of Attorney

As a below named inventor, I hereby declare that:

This declaration is of the following type:

[X] original [ ] supplemental

[X] national stage of PCT

[ ] divisional [ ] continuation [ ] continuation-in-part

My residence, post office address and citizenship are as stated next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

NITROGEN-CONTAINING AROMATIC DERIVATIVES

the specification of which

[ ] is attached hereto.

[ ] was filed on _____
as United States Application Serial Number _____ and,
was amended on _____ (if applicable).

[X] was filed on August 28, 2003
as PCT International Application Number PCT/JP03/10964 and,
was amended under PCT Article 19 on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority under Title 35, United States Code, Section 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATIONS, BENEFIT CLAIMED UNDER 35 USC §119(a)

Application Number	Country	Date of Filing (Day/Month/Year)	Priority Claimed Under 35 USC 119
P2002-253123	Japan	30 / August / 2002	[X] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

PRIOR U.S. PROVISIONAL APPLICATIONS, BENEFIT CLAIMED UNDER 35 USC §119(e)

Application Number	Filing Date
60/464690	22/April/2003

I hereby claim the benefit of Title 35, United States Code Section 120 of any United States application(s), or 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S., BENEFIT CLAIMED UNDER 35 USC §120

(Application No.)	(Filing Date)	(Status: Patented, Pending, Abandoned)
(Application No.)	(Filing Date)	(Status: Patented, Pending, Abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith (list name and registration number or Customer Number)

Send Correspondence to:

CHOATE, HALL & STEWART
Exchange Place 53 State Street

Boston, MA 02109-2891
Direct Telephone Calls to: 617-248-5000/5175

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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ATTORNEY'S DOCKET NUMBER: 2003946-0176

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Tsuruoka *et al.*	Examiner:	N/A
Serial No.:	N/A	Art Unit:	N/A
Filed:	January 12, 2005		
For:	*Nitrogen-Containing Aromatic Derivatives*		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

EXPRESS MAIL NUMBER: EV 416228410 US

Sir:

PRELIMINARY AMENDMENT

Please amend the above-referenced application as follows:

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 5 of this paper.

Remarks begin on page 30 of this paper.

Amendments to the Specification

Please add the following paragraph on page 1 after the title "NITROGEN-CONTAINING AROMATIC DERIVATIVES":

Related Applications

The present application claims priority to PCT application, PCT/JP03/01964, filed August 23, 2003, which claims priority to Japanese patent application 2002-253123, filed August 30, 2002, and U.S. provisional patent application, U.S.S.N. 60/464,690, filed April 22, 2003; each of which is incorporated herein by reference.

Please replace the first three lines of paragraph [0010] on page 4 with the following amended lines:

Specifically, the present invention provides the ~~followings~~ following:

<1> a compound (except N1-cyclopropyl-5-((2(((2-chloroethylamino)carbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide) represented by the general formula:

Please replace the line 18 on page 9 with the following amended line:

<2> a compound (except N1-cyclopropyl-5-((2-(((2-chloroethylamino)carbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide) represented by the general formula:

Please replace the subtitle "**Best mode for carrying out the Invention**" on page 40, line 22, with the following subtitle:

Detailed Description of the Invention

Please replace Table 1 in paragraph [0147] on page 108 with the following amended Table 1:

[Table 1]

Example No.	VEGF-stimulated tube formation IC_{50} (nM)	FGF2-stimulated tube formation IC_{50} (nM)
39	5.1	470
41	2.1	250
46	7.0	470
47	5.8	120
53	6.7	440
78	3.0	450
ref. 1	35	>10000

Please replace Table 2 in paragraph [0153] on page 115 with the following amended Table 2:

[Table 2]

Example No.	VEGFR2 kinase IC_{50} (nM)	FGFR1 kinase IC_{50} (nM)	Example No.	VEGFR2 kinase IC_{50} (nM)	FGFR1 kinase IC_{50} (nM)
7	8.0	26	68	37	52
11	3.0	47	79	9.8	25
18	3.0	70	81	12	38
28	4.5	4.1	82	15	24
32	9.3	16	88	14	24
33	7.1	12	104	3.9	19
34	8.4	22	116	14	87
36	3.4	16	119	21	120
37	4.8	1.2	139	6.3	190
39	4.5	6.3	206	4.1	3.5
40	5.7	6.9	207	4.6	12
41	6.1	3.2	208	7.7	6.8
43	6.4	18	209	17	29
44	7.7	14	210	8.1	40

46	32	12	211	45	36
47	40	21	212	8.6	19
50	5.0	13	213	10	330
53	3.8	2.1	ref. 1	45	600

Please replace paragraph [0516] on page 411 with the following amended paragraph:

~~Example 222~~ Reference Example 1

N1-Cyclopropyl-5-((2-(((2-chloroethylamino)carbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide

N1-cyclopropyl-5-((2-amino-4-pyridyl)oxy)-1H-1-indolecarboxamide (400 mg, CAS No. 417722-12-4) described in WO02/32872, 2-chloroethyl isocyanate (150 mg) and tetrahydrofuran (5 ml) were stirred at 80 °C for 1.5 hours. The mixture was cooled to room temperature, silica gel was added, and the solvent was distilled off under reduced pressure. The silica gel was charged into a dry column packed with silica gel, and purification was performed by column chromatography (hexane : ethyl acetate = 1 : 1, followed by ethyl acetate) to yield 280 mg of a colorless powder.

^{1}H-NMR Spectrum (DMSO-d_6) δ(ppm): 0.57-0.63 (2H, m), 0.70-0.75 (2H, m), 2.73-2.80 (1H, m), 3.42 (2H, q, J= 6.0Hz), 3.61 (2H, t, J= 6.0Hz), 6.52 (1H, dd, J= 5.6Hz, 2.4Hz), 6.65 (1H, d, J= 3.6Hz), 6.85 (1H, d, J= 2.4Hz), 7.04 (1H, dd, J= 8.8Hz, 2.4Hz), 7.35 (1H, d, J= 2.4Hz), 7.86 (1H, d, J= 3.6Hz), 8.04 (1H, d, J= 5.6Hz), 8.27 (1H, s), 8.28 (1H, d, J= 8.8Hz), 8.34 (1H, brs), 9.19 (1H, s).

Please replace paragraph [0517] on page 412 with the following amended paragraph:

The structural formulas of the compounds obtained in ~~Production examples and Examples~~ Production Examples, Examples, and Reference Example above are shown in Tables 5 to 17 below.

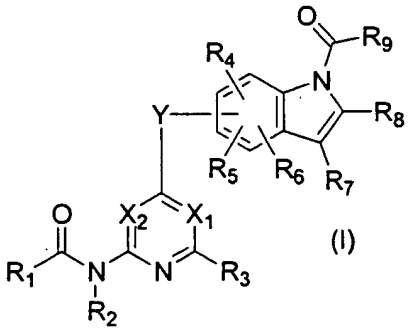
Please replace "Example 222" in Table 17 on page 425, with "Reference Example 1".

Amendments to the Claims

This following Listing of the Claims replaces all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Presently amended) A compound (except N1-cyclopropyl-5-((2-(((2-chloroethylamino)carbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide) represented by the general formula:

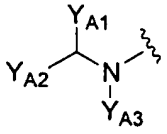


(I)

wherein X_1 represents a nitrogen atom or a group represented by the formula $-CR_{10}=$, X_2 represents a nitrogen atom or a group represented by the formula $-CR_{11}=$, and X_1 and X_2 do not represent a nitrogen atom at the same time;

Y represents an oxygen atom, a sulfur atom, a sulfinyl group, a sulfonyl group, or a group represented by the formula $-NR_Y-$ (wherein R_Y represents a hydrogen atom or a C_{1-6} alkyl group);

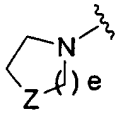
R_1 represents an optionally substituted C_{1-6} alkoxy group, an optionally substituted C_{6-10} aryloxy group, a group represented by the formula $-NR_{12a}R_{12b}$, a group represented by the formula:



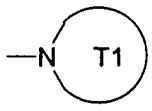
(VIII)

(wherein Y_{A1} and Y_{A2} each independently represent a group represented by the formula $-A_{10}-A_{11}-A_{12}$ (wherein A_{10} represents a single bond or an optionally substituted C1-6 alkylene; A_{11} represents a single bond, an oxygen atom, a carbonyl group or a sulfonyl group; and A_{12} represents a hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{3-8}

cycloalkyl group, a C_{6-10} aryl group, a 5- to 10- membered heteroaryl group, a group represented by the formula $-NR_{A10}R_{A11}$, a group represented by the formula $-OR_{A12}$ (wherein R_{A10}, R_{A11} and R_{A12} each independently represent a hydrogen atom, a C1-6 alkyl group or C_{3-8} cycloalkyl group) or a group represented by the formula:



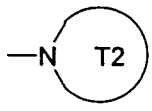
(wherein e represents 1 or 2; Z represents an oxygen atom, a group represented by the formula $-CR_{X7}R_{X8}-$ or a group represented by the formula $-NR_{X9}-$; R_{X7}, R_{X8} and R_{X9} each independently represent a hydrogen atom, a hydroxyl group or a C_{1-6} alkyl group)); and Y_{A3} represents a hydrogen atom or an optionally substituted C_{1-6} alkyl group) or a group represented by the formula:



(wherein T1 represents an optionally substituted 5- to 10- membered aromatic heterocycle which may have X in the ring or an optionally substituted 3- to 10- membered heterocycle which may have X in the ring);

R_3, R_4, R_5, R_6, R_7, R_8, R_{10} and R_{11} each independently represent a hydrogen atom, a halogen atom, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{2-6} alkenyl group, an optionally substituted C_{2-6} alkynyl group, an optionally substituted C_{3-8} cycloalkyl group, a group represented by the formula $-CO-R_{13}$, a group represented by the formula $-NR_{14}-CO-R_{13}$, a group represented by the formula $-SO_2-R_{15}$, a group represented by the formula $-NR_{14}-SO_2-R_{15}$, or a group represented by the formula $-NR_{16a}R_{16b}$;

R_9 represents a group represented by the formula $-NR_{16a}R_{16b}$ or a group represented by the formula:

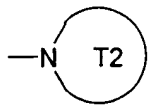


(wherein T2 represents an optionally substituted 5- to 10- membered aromatic heterocycle or an optionally substituted 3- to 10- membered heterocycle);

R_{12a} and R_{12b} each independently represent a hydrogen atom, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-6} alkenyl group, an optionally substituted C_{3-6} alkynyl group,

an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted 3- to 10- membered heterocyclic group, or an optionally substituted C_{1-6} alkoxy group;

R_{13} represents a hydrogen atom, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{2-6} alkenyl group, an optionally substituted C_{2-6} alkynyl group, an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted C_{6-10} aryl group, an optionally substituted 5- to 10- membered heteroaryl group, an optionally substituted 3- to 10- membered heterocyclic group, an optionally substituted C_{1-6} alkoxy group, an optionally substituted C_{6-10} aryloxy group, a group represented by the formula $-NR_{12a}R_{12b}$, or a group represented by the formula:



(wherein T2 represents an optionally substituted 5- to 10- membered aromatic heterocycle or an optionally substituted 3- to 10- membered heterocycle);

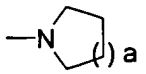
R_2 and R_{14} each independently represent a hydrogen atom, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{2-6} alkenyl group, an optionally substituted C_{2-6} alkynyl group, an optionally substituted C_{3-8} cycloalkyl group, or a group represented by the formula $-CO-R_{13}$;

R_{15} represents an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{2-6} alkenyl group, an optionally substituted C_{2-6} alkynyl group, an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted C_{6-10} aryl group, an optionally substituted 5- to 10- membered heteroaryl group, or an optionally substituted 3- to 10- membered heterocyclic group;

R_{16a} and R_{16b} each independently represent a hydrogen atom, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-6} alkenyl group, an optionally substituted C_{3-6} alkynyl group, an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted C_{6-10} aryl group, an optionally substituted 5- to 10- membered heteroaryl group, an optionally substituted 3- to 10- membered heterocyclic group, or an optionally substituted C_{1-6} alkoxy group; and

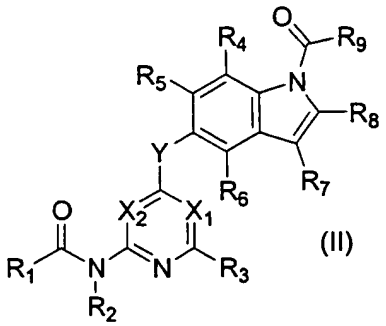
X represents an oxygen atom, a sulfur atom, a carbonyl group, a sulfonyl group, a group represented by the formula $-CR_{X1}R_{X2}-$, or a group represented by the formula $-NR_{X3}-$ (wherein R_{X1}, R_{X2} and R_{X3} each independently represent a hydrogen atom or a group represented by the formula $-A_1-A_2-A_3$ (wherein A_1 and A_2 each independently represent a single bond, an optionally substituted C_{1-6} alkylene group or a carbonyl group; and A_3 represents a hydrogen

atom, a C_{3-8} cycloalkyl group, a group represented by the formula $-NR_{A1}R_{A2}$, or the formula $-OR_{A3}$ (wherein, R_{A1}, R_{A2} and R_{A3} each independently represent a hydrogen atom or a C_{1-6} alkyl group), or an optionally substituted group represented by the formula:



(wherein a represents 1 or 2))),
a salt thereof, or a hydrate of the foregoing.

2. (Presently amended) ~~A~~ The compound of claim 1 (except N1-cyclopropyl-5-((2-(((2-chloroethylamino)carbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide) represented by the general formula:



(II)

wherein X_1, X_2, Y, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 represent the same definitions as X_1, X_2, Y, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 in claim 1, respectively,
a salt thereof, or a hydrate of the foregoing.

3. (Presently amended) ~~A~~ The compound according to claim 1 ~~or 2~~, a salt of the compound, or a hydrate of the foregoing, wherein Y represents an oxygen atom, a group represented by the formula –NH-, or a group represented by the formula $-N(CH_3)-$.

4. (Presently amended) ~~A~~ The compound according to claim 1 ~~or 2~~, a salt of the compound, or a hydrate of the foregoing, wherein Y represents an oxygen atom.

5. (Presently amended) ~~A~~ The compound according to any of claims 1 ~~to 4~~, a salt of the compound, or a hydrate of the foregoing, wherein one of X_1 and X_2 represents a group represented by the formula –CH= and the other represents a nitrogen atom.

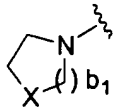
6. (Presently amended) ~~A~~ The compound according to any of claims 1 ~~to 4,~~ a salt of the compound, or a hydrate of the foregoing, wherein both X_1 and X_2 represent a group represented by the formula –CH=.

7. (Presently amended) ~~A~~ The compound according to any of claims 1 ~~to 6~~, a salt of the compound, or a hydrate of the foregoing, wherein R_3, R_4, R_5, R_6 and R_8 each represent a hydrogen atom, and R_7 represents a hydrogen atom, a halogen atom or an optionally substituted C_{1-6} alkyl group.

8. (Presently amended) ~~A~~ The compound according to any of claims 1 ~~to 7~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula $-NHR_{17}$ (wherein R_{17} represents an optionally substituted C_{1-6} alkyl group, a C_{3-6} alkynyl group, a C_{3-8} cycloalkyl group, an optionally substituted C_{6-10} aryl group or an optionally substituted 5- to 10- membered heteroaryl group).

9. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 7~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula $-NR_{18a}R_{18b}$ (wherein R_{18a} and R_{18b} each independently represent a C_{1-6} alkyl group).

10. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 7~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula:



(III)

(wherein b_1 represents 1 or 2; X represents the same definition as X in claim 1).

11. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 7~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula $-NHR_{19}$ (wherein R_{19} represents a C_{1-6} alkyl group, a C_{3-6} alkynyl group, a C_{3-8}

cycloalkyl group or a C_{6-10} aryl group).

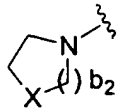
12. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 11~~, a salt of the compound, or a hydrate of the foregoing, wherein R_3, R_4, R_5, R_6, R_7 and R_8 each represent a hydrogen atom.

13. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 12~~, a salt of the compound, or a hydrate of the foregoing, wherein R_2 represents a hydrogen atom.

14. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 13~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula $-NHR_{20}$ (wherein R_{20} represents a methyl group, an ethyl group or a cyclopropyl group).

15. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 13~~, a salt of the compound, or a hydrate of the foregoing, wherein R_9 represents a group represented by the formula $-NH(CH_3)$.

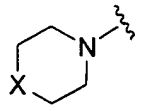
16. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a further optionally substituted group represented by the formula:



(III')

(wherein b_2 represents 0, 1 or 2; and X represents the same definition as X in claim 1).

17. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 16~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formula:

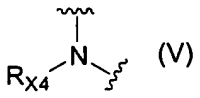


(IV)

(wherein X represents the same definition as X in claim 1).

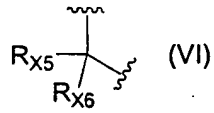
18. (Presently amended) ~~A~~ The compound according to claim 17, a salt of the compound, or a hydrate of the foregoing, wherein X in the formula (IV) represents an oxygen atom.

19. (Presently amended) ~~A~~ The compound according to claim 17, a salt of the compound, or a hydrate of the foregoing, wherein X in the formula (IV) represents a group represented by the formula:

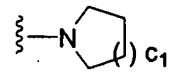

(V)

(wherein R_{X4} represents a hydrogen atom or a group represented by the formula $-A_4-A_5-A_6$ (wherein A_4 and A_5 each independently represent a single bond, an optionally substituted C_{1-6} alkylene or a carbonyl group; and A_6 represents a hydrogen atom, a C_{3-8} cycloalkyl group or a group represented by the formula $-NR_{A4}R_{A5}$ or the formula $-OR_{A6}$ (wherein R_{A4}, R_{A5} and R_{A6} each independently represent a hydrogen atom or a C_{1-6} alkyl group))).

20. (Presently amended) ~~A~~ The compound according to claim 17, a salt of the compound, or a hydrate of the foregoing, wherein X in the formula (IV) represents a group represented by the formula:


(VI)

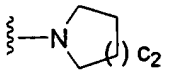
(wherein R_{X5} and R_{X6} each independently represent a hydrogen atom or a group represented by the formula $-A_7-A_8-A_9$ (wherein A_7 and A_8 each independently represent a single bond, an optionally substituted C_{1-6} alkylene group or a carbonyl group; and A_9 represents a hydrogen atom, a C_{3-8} cycloalkyl group, a group represented by the formula $-NR_{A7}R_{A8}$, or the formula $-OR_{A9}$ (wherein R_{A7}, R_{A8}, and R_{A9} each independently represent a hydrogen atom or a C_{1-6} alkyl group), or a group represented by the formula:



(wherein c_1 represents 0, 1 or 2))).

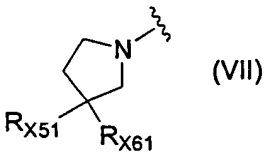
21. (Presently amended) ~~A~~ The compound according to claim 20, a salt of the compound, or a hydrate of the foregoing, wherein one of R_{X5} and R_{X6} in the formula (VI) represents a hydroxyl group and the other represents a hydrogen atom or a C_{1-6} alkyl group.

22. (Presently amended) ~~A~~ The compound according to claim 20, a salt of the compound, or a hydrate of the foregoing, wherein one of R_{X5} or R_{X6} in the formula (VI) represents a hydrogen atom and the other represents a group represented by the formula:



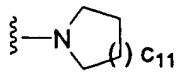
(wherein c_2 represents 1 or 2).

23. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 16~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formula:



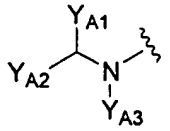
(VII)

(wherein R_{X51} and R_{X61} each independently represent a hydrogen atom or a group represented by the formula $-A_{71}$-A_{81}-A_{91} (wherein A_{71} and A_{81} each independently represent a single bond, an optionally substituted C_{1-6} alkylene group or a carbonyl group; and A_{91} represents a hydrogen atom, a C_{3-8} cycloalkyl group, a group represented by the formula $-NR_{A71}R_{A81}$, or the formula $-OR_{A91}$ (wherein R_{A71}, R_{A81}, and R_{A91} each independently represent a hydrogen atom or a C_{1-6} alkyl group), or a group represented by the formula:

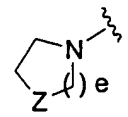


(wherein c_{11} represents 0, 1 or 2))).

24. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formula:

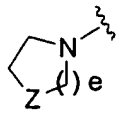

(VIII)

(wherein Y_{A1} and Y_{A2} each independently represent a group represented by the formula $-A_{10}$-A_{11}-A_{12} (wherein A_{10} represents a single bond or an optionally substituted C_{1-6} alkylene group; A_{11} represents a single bond, an oxygen atom, a carbonyl group, or a sulfonyl group; and A_{12} represents a hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{3-8} cycloalkyl group, a C_{6-10} aryl group, a 5- to 10- membered heteroaryl group, a group represented by the formula $-NR_{A10}R_{A11}$, or the formula $-OR_{A12}$ (wherein, R_{A10}, R_{A11} and R_{A12} each independently represent a hydrogen atom, a C_{1-6} alkyl group or a C_{3-8} cycloalkyl group), or a group represented by the formula:



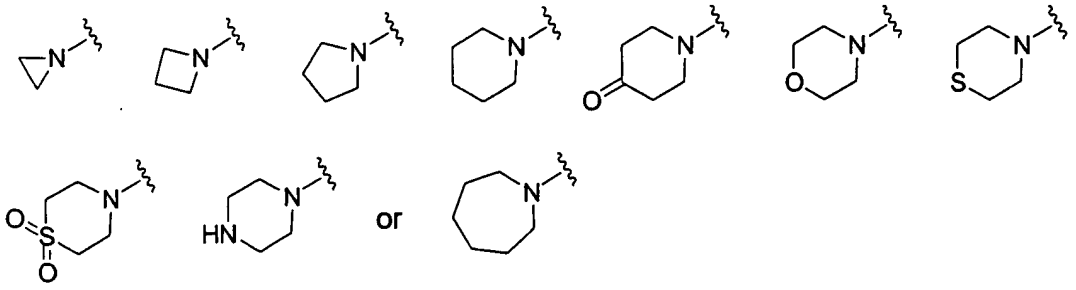
(wherein e represents 1 or 2; and Z represents an oxygen atom or a group represented by the formula $-CR_{X7}R_{X8}-$ or the formula $-NR_{X9}-$ (wherein R_{X7}, R_{X8} and R_{X9} each independently represent a hydrogen atom, a hydroxyl group or a C_{1-6} alkyl group))); and Y_{A3} represents a hydrogen atom or an optionally substituted C_{1-6} alkyl group).

25. (Presently amended) ~~A~~ The compound according to claim 24, a salt of the compound, or a hydrate of the foregoing, wherein one of Y_{A1} and Y_{A2} in the formula (VIII) represents a hydrogen atom and the other represents a group represented by the formula $-(CH_2)_2$-A_{13}-A_{14} (wherein A_{13} represents a single bond, a carbonyl group or a sulfonyl group; and A_{14} represents a C_{1-6} alkyl group, a group represented by the formula $-NR_{A13}R_{A14}$ (wherein R_{A13} and R_{A14} each independently represent a hydrogen atom, a C_{1-6} alkyl group or a C_{3-8} cycloalkyl group), or a group represented by the formula:



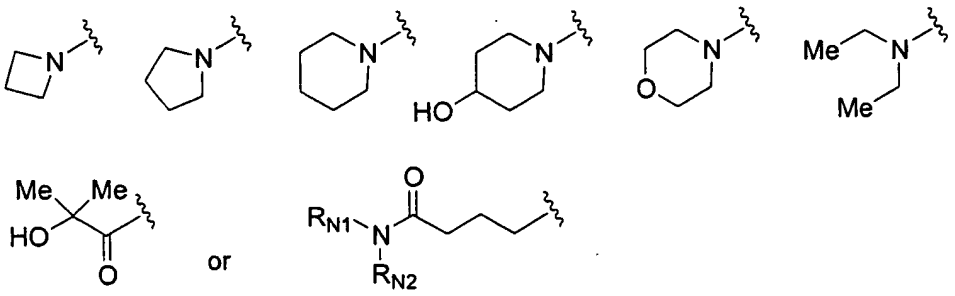
(wherein e and Z represent the same definitions as e and Z in claim 24, respectively)); and Y_{A3} in the formula (VIII) represents a hydrogen atom.

26. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formulas:



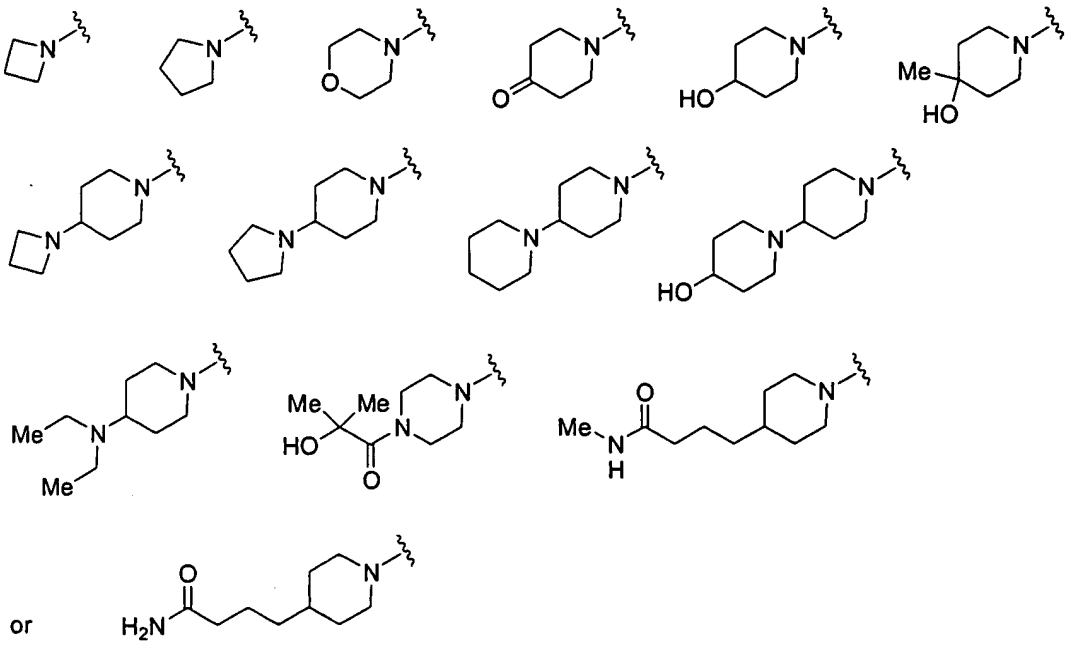
(each of the foregoing members being optionally substituted with a group selected from Substituent Group Alpha,

wherein Substituent Group Alpha is a group consisting of a halogen atom, a hydroxyl group, a thiol group, a nitro group, a cyano group, a carboxyl group, an amino group, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, and a group represented by the formulas:



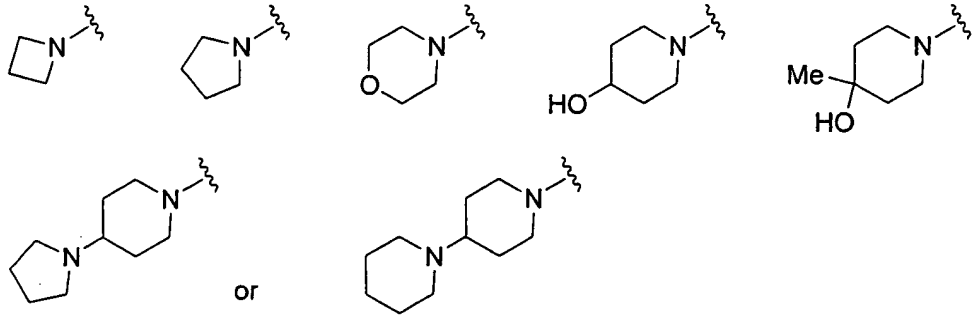
(wherein R_{N1} and R_{N2} each independently represent a hydrogen atom or a C_{1-6} alkyl group)).

27. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formulas:



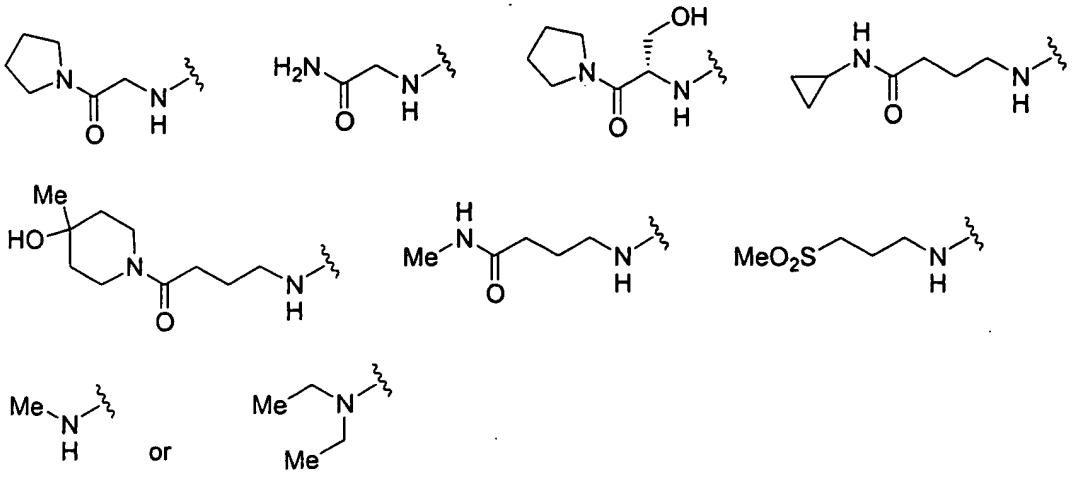
or

28. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formulas:

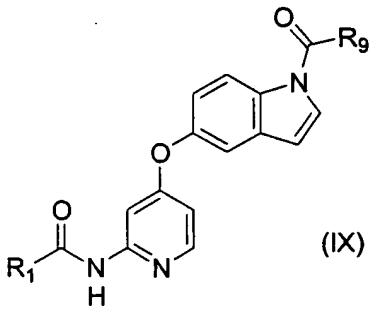


or

29. (Presently amended) ~~A~~ The compound according to claim 1 ~~any of claims 1 to 15~~, a salt of the compound, or a hydrate of the foregoing, wherein R_1 represents a group represented by the formulas:

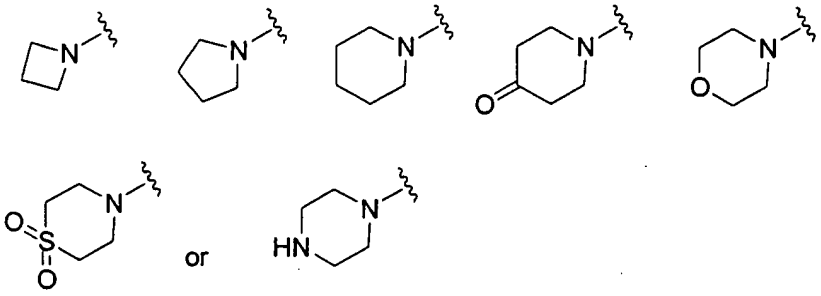


30. (Presently amended) ~~A~~ The compound according to claim 1 ~~or 2~~, a salt of the compound, or a hydrate of the foregoing, wherein the compound is represented by the general formula:



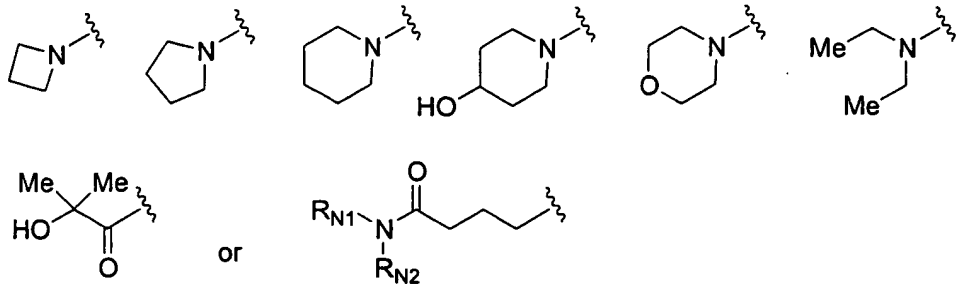
(IX)

(wherein R_1 represents a group represented by the formulas:



(each of the foregoing members being optionally substituted with a group selected from Substituent Group Beta,

wherein Substituent Group Beta is a group consisting of a hydroxyl group, a C_{1-6} alkyl group, a C_{3-8} cycloalkyl group, and a group represented by the formulas:



(wherein R_{N1} and R_{N2} each independently represent a hydrogen atom or a C_{1-6} alkyl group)); and R_9 represents a group represented by the formula $-NHR_{20}$ (wherein R_{20} represents a methyl group, an ethyl group or a cyclopropyl group)).

31. (Presently amended) ~~A~~ The compound according to claim 1, a salt of the compound, or a hydrate of the foregoing, wherein the compound is a compound selected from a group consisting of

(1) N1-ethyl-5-(2-((methoxylamino)carbonyl)amino-4-pyrimidyl)oxy-1H-indolecarboxamide;

(2) 5-(6-(3-(3-diethylaminopropylamino)ureido)pyrimidin-4-yloxy)–1H-indole-1-carboxylic acid methylamide;

(3) 5-(6-(((4-hydroxypiperidin-1-yl)carbonyl)amino)-pyrimidin-4-yloxy)–1H-indole-1-carboxylic acid methylamide;

(4) 5-(6-((4-pyrrolidin-1-yl)piperidin-1-yl)carbonylamino)pyrimidin-4-yloxy)–1H-indole-1-carboxylic acid methylamide;

(5) 5-(2-(3-((1R)–1-carbamoyl-2-phenylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(6) 5-(2-(3-((1S)-1-carbamoyl-2-phenylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(7) 5-(2-(3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(8) 5-(2-(3-(2-(4-hydroxy-4-methylpiperidin-1-yl)-2-oxoethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(9) 5-(2-(3-((1S)-1-carbamoylethyl)ureido)pyridin-4-yloxy)–1H-indole-1-carboxylic acid methylamide;

(10) 5-(2-(3-((1S)-1-carbamoyl-3-methylbutyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic

acid methylamide;

(11) 5-(2-(3-carbamoylmethylureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(12) 5-(2-(3-cyclopropylcarbamoylmethylureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(13) 5-(2-(3-((1S)–1-carbamoyl-2-hydroxyethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(14) 5-(2-(3-((1R)-1-carbamoyl-2-hydroxyethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(15) (2S)-2-(3-(4-(1-methylcarbamoyl-1H-indol-5-yloxy)pyridin-2-yl)ureido)-1,5-pentanedicarboxylic acid diamide;

(16) (2S)–2-(3-(4-(1-methylcarbamoyl-1H-indol-5-yloxy)pyridin-2-yl)ureido)succinamide;

(17) 5-(2-(3-((1S)-1-cyclopropylcarbamoyl-2-hydroxyethyl)ureido)pyridin-4-yloxy)–1H-indole-1-carboxylic acid methylamide;

(18) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(19) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(20) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(21) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(22) 5-(2-(3-((1S)-1-hydroxymethyl-2-(4-hydroxypiperidin-1-yl)-2-oxoethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(23) 5-(2-(3-((1S)-1-hydroxymethyl-2-(morpholin-4-yl)-2-oxoethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(24) 5-(2-(3-(2-cyclopropylcarbamoylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(25) 5-(2-(3-(3-oxo-3-(pyrrolidin-1-yl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(26) 5-(2-(3-(3-(4-hydroxy-4-methylpiperidin-1-yl)-3-oxopropyl)ureido)pyridin-4-yloxy)-1H-

indole-1-carboxylic acid methylamide;

(27) N1-ethyl-5-(2-(((2-ethoxyethyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(28) N1-methyl-5-(2-((4-(2-hydroxy-2-methylpropionyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(29) N1-methyl-5-(2-((3-(diethylamino)propylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(30) N1-methyl-5-(2-(((3-(4-hydroxypiperidino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(31) N1-methyl-5-(2-(((3-(4-methylpiperazin-1-yl)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(32) 5-(2-(3-(4-oxo-4-(pyrrolidin-1-yl)butyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(33) 5-(2-(3-(3-(cyclopropylcarbamoyl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(34) 5-(2-(3-(4-(4-hydroxy-4-methylpiperidin-1-yl)-4-oxobutyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(35) 5-(2-(3-(3-(diethylcarbamoyl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(36) 5-(2-(3-(3-(methylcarbamoyl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(37) N1-methyl-5-(2-(pyrrolidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(38) N1-methyl-5-(2-(piperidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(39) N1-methyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(40) N1-methyl-5-(2-(4-oxopiperidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(41) 5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(42) N1-methyl-5-(2-((4-(1-hydroxy-1-methylethyl)piperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(43) 5-(2-(((4-(3-methylcarbamoylpropyl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(44) 5-(2-(((4-(3-carbamoylpropyl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(45) 5-(2-((4-((pyrrolidin-1-yl)carbonyl)piperidin-1-yl)carbonylamino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(46) N1-methyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(47) N1-methyl-5-(2-(((4-(piperidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(48) N1-methyl-5-(2-((4-ethylpiperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(49) N1-methyl-5-(2-((4-(2-hydroxyethyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(50) N1-methyl-5-(2-((3-methylsulfonylpropylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(51) N1-methyl-5-(2-((4-(2-dimethylaminoacetyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(52) N1-methyl-5-(2-((4-cyclohexylpiperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(53) N4-(4-(1-(methylamino)carbonyl-1H-5-indolyl)oxy-2-pyridyl)-4-morpholinecarboxamide;

(54) N1-methyl-5-(2-((1,1-dioxothiomorpholin-4-ylcarbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(55) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(56) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(57) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(58) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(59) 5-(2-(3-(2-(4-hydroxy-4-methylpiperidin-1-yl)-2-oxoethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(60) N1-ethyl-5-(2-((((1-methyl-4-piperidyl)methyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(61) N1-ethyl-5-(2-(((2-diethylamino)ethyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(62) N1-ethyl-5-(2-(((2-(morpholin-4-yl)ethyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(63) N1-ethyl-5-(2-(((2-(4-hydroxypiperidino)ethyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(64) N1-methyl-5-(2-(((2-(4-hydroxypiperidino)ethyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(65) N1-ethyl-5-(2-((3-(diethylamino)propylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(66) N1-ethyl-5-(2-(((3-(morpholin-4-yl)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(67) N1-ethyl-5-(2-(((3-(4-methylpiperazin-1-yl)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(68) N1-cyclopropyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(69) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopropylamide;

(70) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopropylamide;

(71) 5-(2-(3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopropylamide;

(72) 5-(2-(3-(3-oxo-3-(pyrrolidin-1-yl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopropylamide;

(73) 5-(2-(3-((1R)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopropylamide;

(74) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-piperidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-

indole-1-carboxylic acid cyclopropylamide;

(75) N1-phenyl-5-(2-(((3-(diethylamino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(76) N1-phenyl-5-(2-(((3-(4-methylpiperazin-1-yl)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(77) N1-ethyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(78) 5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(79) N1-ethyl-5-(2-((4-hydroxypiperidin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(80) N1-ethyl-5-(2-(piperidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(81) N1-ethyl-5-((2-((pyrrolidin-1-ylcarbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide;

(82) N4-(4-((1-(ethylamino)carbonyl-1H-5-indolyl)oxy)–2-pyridyl)–4-morpholinecarboxamide;

(83) N1-ethyl-5-(2-((1,1-dioxothiomorpholin-4-ylcarbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(84) N1-ethyl-5-(2-((methoxylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(85) N1-cyclopropyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(86) N1-cyclopropyl-5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarbox-amide;

(87) N4-(4-(1-(cyclopropylamino)carbonyl-1H-5-indolyl)oxy-2-pyridyl)–4-morpholinecarboxamide;

(88) N1-cyclopropyl-5-(2-((pyrrolidin-1-ylcarbonyl)amino)-4-pyridyl)oxy-1H-1-indolecarboxamide;

(89) N1-cyclopropyl-5-(2-(piperidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(90) N4-(4-(1-(cyclopentylamino)carbonyl-1H-5-indolyl)oxy–2-pyridyl)–4-morpholinecarboxamide;

(91) 5-(2-(((4-hydroxypiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid cyclopentylamide;

(92) N1-cyclopentyl-5-(2-((4-(pyrrolidin-1-yl)piperidin-1-ylcarbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(93) N1-(3-methylbutyl)-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(94) N1-(3-methylbutyl)-5-(2-((4-(hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(95) N4-(4-(1-((3-methylbutyl)amino)carbonyl-1H-5-indolyl)oxy–2-pyridyl)–4-morpholinecarboxamide;

(96) N1-(1-ethylpropyl)-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(97) N1-(1-ethylpropyl)-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(98) N4-(4-(1-((1-ethylpropyl)amino)carbonyl-1H-5-indolyl)oxy–2-pyridyl)–4-morpholinecarboxamide;

(99) N4-(4-(1-((1-pentyl)amino)carbonyl-1H-5-indolyl)oxy–2-pyridyl)–4-morpholinecarboxamide;

(100) N1-(1-pentyl)-5-(2-(((4-hydroxypiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(101) N1-(1-pentyl)-5-(2-((4-(pyrrolidin-1-yl)piperidin-1-ylcarbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(102) N1-methyl-3-chloro-5-(2-(((3-(diethylamino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(103) N1-methyl-3-chloro-5-(2-((4-(pyrrolidin-1-yl)piperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(104) N1-methyl-3-chloro-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(105) N1-methyl-3-chloro-5-(2-(((3-(4-hydroxypiperidino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(106) N1-methyl-3-chloro-5-(2-((4-(2-hydroxyethyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(107) N4-(4-(3-chloro-1-(methylamino)carbonyl-1H-5-indolyl)oxy–2-pyridyl)–4-

morpholinecarboxamide;

(108) N1-methyl-3-chloro-5-(2-((4-(ethylpiperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(109) N1-ethyl-3-chloro-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(110) N1-ethyl-3-chloro-5-(2-(((3-(4-hydroxypiperidino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(111) N1-ethyl-3-chloro-5-(2-(((3-(diethylamino)propyl)amino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(112) N1,3-dimethyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(113) N1,3-dimethyl-5-(2-((4-(pyrrolidin-1-yl)piperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(114) N1-cylopropyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-3-methyl-1H-1-indolecarboxamide;

(115) N1-cylopropyl-5-(2-((4-(2-hydroxyethyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-3-methyl-1H-1-indolecarboxamide;

(116) N1-methyl-5-(2-((methylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(117) N1-methyl-5-(2-((diethylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(118) N1-(2-propynyl)-5-(2-((pyrrolidin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(119) N1-methyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(120) N1-ethyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(121) N1-cyclopropyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(122) N1-methyl-5-(2-(((4-(morpholin-4-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(123) N1-methyl-5-(2-(((4-(azetidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(124) N1-methyl-5-(2-(((4-(diethylamino)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(125) N1-methyl-5-(2-(((4-(4-hydroxypiperidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide; and

(126) N1-propyl-5-(2-(pyrrolidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide.

32. (Presently amended) ~~A~~ The compound according to claim 1, a salt of the compound, or a hydrate of the foregoing, wherein the compound is a compound selected from a group consisting of

(1) 5-(2-(3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(2) 5-(2-(3-carbamoylmethylureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(3) 5-(2-(3-((1S)-1-hydroxymethyl-2-oxo-2-pyrrolidin-1-ylethyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(4) N1-methyl-5-(2-((4-(2-hydroxy-2-methylpropionyl)piperazin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(5) 5-(2-(3-(4-oxo-4-(pyrrolidin-1-yl)butyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(6) 5-(2-(3-(3-(cyclopropylcarbamoyl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(7) 5-(2-(3-(4-(4-hydroxy-4-methylpiperidin-1-yl)-4-oxobutyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(8) 5-(2-(3-(3-(methylcarbamoyl)propyl)ureido)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(9) N1-methyl-5-(2-(pyrrolidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(10) N1-methyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(11) N1-methyl-5-(2-(4-oxopiperidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(12) 5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(13) 5-(2-(((4-(3-methylcarbamoylpropyl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(14) 5-(2-(((4-(3-carbamoylpropyl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;

(15) N1-methyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(16) N1-methyl-5-(2-(((4-(piperidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(17) N1-methyl-5-(2-((3-methylsulfonylpropylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(18) N4-(4-(1-(methylamino)carbonyl-1H-5-indolyl)oxy-2-pyridyl)-4-morpholinecarboxamide;

(19) N1-cyclopropyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(20) 5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid ethylamide;

(21) N1-ethyl-5-(2-((4-hydroxypiperidin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(22) N1-ethyl-5-((2-((pyrrolidin-1-ylcarbonyl)amino)-4-pyridyl)oxy)-1H-1-indolecarboxamide;

(23) N4-(4-((1-(ethylamino)carbonyl-1H-5-indolyl)oxy)-2-pyridyl)-4-morpholinecarboxamide;

(24) N1-cyclopropyl-5-(2-((pyrrolidin-1-ylcarbonyl)amino)-4-pyridyl)oxy-1H-1-indolecarboxamide;

(25) N1-methyl-3-chloro-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(26) N1-methyl-5-(2-((methylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(27) N1-methyl-5-(2-((diethylamino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(28) N1-(2-propynyl)-5-(2-((pyrrolidin-1-yl)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(29) N1-methyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(30) N1-ethyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(31) N1-cyclopropyl-5-(2-(azetidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;

(32) N1-methyl-5-(2-(((4-(morpholin-4-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;

(33) N1-methyl-5-(2-(((4-(azetidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-

indolecarboxamide;
(34) N1-methyl-5-(2-(((4-(diethylamino)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;
(35) N1-methyl-5-(2-(((4-(4-hydroxypiperidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide; and
(36) N1-propyl-5-(2-(pyrrolidin-1-ylcarbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide.

33. (Presently amended) ~~A~~ The compound according to claim 1, a salt of the compound, or a hydrate of the foregoing, wherein the compound is a compound selected from a group consisting of
(1) 5-(2-(((4-hydroxy-4-methylpiperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-indole-1-carboxylic acid methylamide;
(2) N1-methyl-5-(2-((4-hydroxypiperidino)carbonyl)amino-4-pyridyl)oxy-1H-1-indolecarboxamide;
(3) N1-methyl-5-(2-(((4-(pyrrolidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide;
(4) N1-methyl-5-(2-(((4-(piperidin-1-yl)piperidin-1-yl)carbonyl)amino)pyridin-4-yloxy)-1H-1-indolecarboxamide; and
(5) N4-(4-(1-(methylamino)carbonyl-1H-5-indolyl)oxy-2-pyridyl)-4-morpholinecarboxamide.

34. (Presently amended) A pharmaceutical composition comprising a compound according to claim 1 ~~any of claims 1 to 33~~ and a pharmaceutical adjuvant.

35. (Presently amended) A prophylactic or therapeutic agent for a disease for which angiogenesis inhibition is effective, comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

36. (Presently amended) An angiogenesis inhibitor comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

37. (Presently amended) An antitumor agent comprising as an active ingredient, a compound according to claim 1, a salt thereof, or a hydrate of the foregoing.

38. (Presently amended) ~~An~~ The antitumor agent according to claim 37, wherein the tumor is a pancreatic cancer, a gastric cancer, a colon cancer, a breast cancer, a prostate cancer, a lung cancer, a renal cancer, a brain tumor, a blood cancer or an ovarian cancer.

39. (Presently amended) A therapeutic agent for hemangioma comprising as an active ingredient , a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

40. (Presently amended) A cancer metastasis inhibitor comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

41. (Presently amended) A therapeutic agent for retinal neovascularization or diabetic retinopathy comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

42. (Presently amended) A therapeutic agent for an inflammatory disease comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

43. (Presently presented) ~~A~~ The therapeutic agent for an inflammatory disease according to claim 42, wherein the inflammatory disease is deformant arthritis, rheumatoid arthritis, psoriasis or delayed hypersensitivity reaction.

44. (Presently amended) A therapeutic agent for atherosclerosis comprising as an active ingredient, a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

45. (Presently amended) A prophylactic or therapeutic method for a disease for which angiogenesis inhibition is effective, comprising administering to a patient, a pharmacologically effective dose of a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing.

46. (Presently amended) Use of a compound according to claim 1 ~~any of claims 1 to 33~~, a salt thereof, or a hydrate of the foregoing for the manufacture of a prophylactic or therapeutic agent for a disease for which angiogenesis inhibition is effective.

Remarks

Applicant respectfully requests entrance of the amendments in the application filed. The amendments to the specification, as detailed above, merely seek to place the application in conformance with United States practice. The claims have been amended to place the claims in conformance with U.S. practice and to reduce claim fees. It is requested that the claim fees be calculated after entrance of the present amendment. Applicant respectfully submits that no new matter is presented with these amendments..

Applicant would like to thank the Examiner in advance for review of this request. If it is believed that a telephone conversation would expedite matters, the Examiner is invited to contact the undersigned at (617) 248-5215.

Respectfully Submitted,

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